

**LEMBAR
HASIL PENILAIAN SEJAWAT SEBIDANG ATAU PEER REVIEW
KARYA ILMIAH : JURNAL ILMIAH**

Judul Jurnal Ilmiah (Artikel)	:	Relationship Between Phylogenetic of <i>Apium</i> and <i>Foeniculum</i> Plants from Central Java, Indonesia, and Their Secondary Metabolites Potency against COVID-19 Protease
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Status Pengusul	:	Penulis pertama
Identitas Jurnal Ilmiah	:	a. Nama Jurnal : Open Access Macedonian Journal of Medical Sciences (OAMJMS) b. Nomor ISSN : 18579655 c. Volume, nomor, bulan, tahun d. Penerbit : Macedonia e. DOI artikel (jika ada) : https://doi.org/10.3889/oamjms.2022.9852 f. Alamat web jurnal : https://oamjms.eu/index.php/mjms/article/view/9852/7814 g. Terindeks di SCOPUS, Q3, SJR 2021 0.26, H Indeks 23
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				17.898

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Semarang, 27 April 2023
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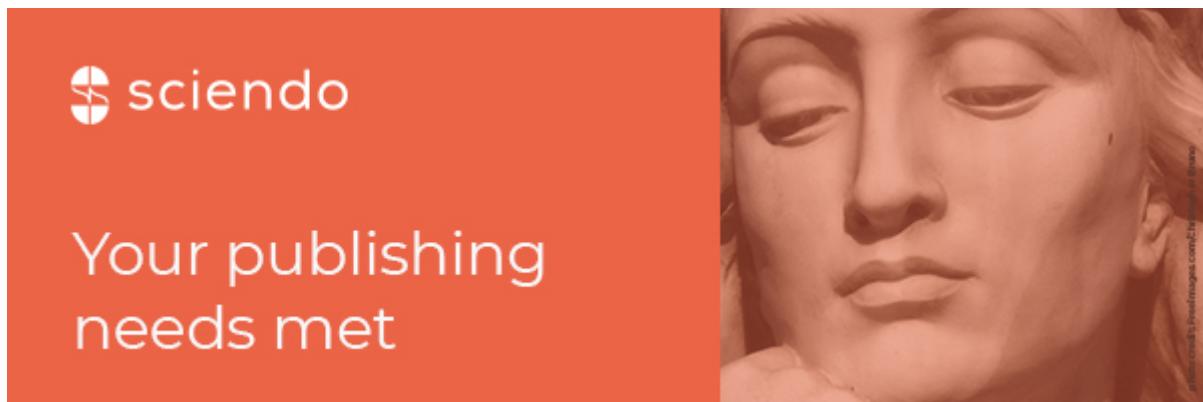
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Antidiabetic Effect Test of Insulin Stem Extract (*Tithonia diversifolia*) Toward Streptozotocin-Induced Diabetic Rats (*Rattus Norvegicus*)

Suherman Suherman, Baharuddin Hamzah, Sri Hastuti V. Pulukadang, Sitti Rahmawati, Muhammad Fakhrul Hardan, Ririen Hardani, Andi Saifah (Author)

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Low-dose Indonesian Aloe vera Increases Viability and Migration of the Fibroblast: An In Vitro Study

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Determination of Total Phenolic Content, Analysis of Bioactive Compound Components, and Antioxidant Activity of Ethyl Acetate Seri (*Muntingia calabura* L.) Leaves from North Sumatera Province, Indonesia

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Preparation and Physicochemical Characterizations of p-Methoxycinnamic acid - Succinic Acid Cocrystal by Solvent Evaporation Technique

Melanny Ika Sulistyowaty, Dwi Setyawan, Retno Sari, Abhimata Paramanandana, Nofika Agung Maharani, Timbul Partogi Simorangkir (Author)

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The Potential of Centella asiatica Herb and Cyperus rotundus L. Rhizomes Extract as a Chemoprevention Agent for Lung Cancer

Indrayanti Indrayanti, Titiek Hidayati, Arif B. Setyanto (Author)

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Chartolepis intermedia Boiss. and Centaurea ruthenica Lam. – New Medicinal Plants Containing Pharmacologically Active Compounds

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The Activity of Combination of Ethanol Extract of *Artocarpus lacucha* Buch.-Ham and *Anredera cordifolia* Steenis Leaves to Increase Wound Healing Process on NIH-3T3 Cell Line

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Artocarpus altilis Extract Capsules Reduce Fasting Blood Glucose in Prediabetes

Junedji Sitorus, Veni Hadju, Nurhaedra Jafar, Ridwan Amiruddin, Aminuddin Syam, Trias Mahmudiono, Yulia Yusriini Djibar, Apik Indarty Moedjiono (Author)

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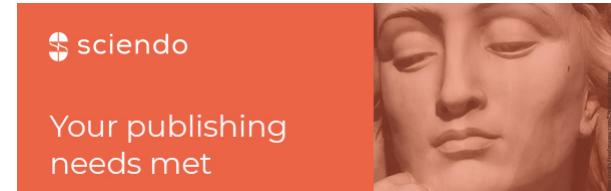
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Peculiarities of Action of Catecholamines and their Metabolites in the Regulation of Cardiomyocyte Enzymes

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Abstract

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BACKGROUND: Myocardial ischemia is accompanied by a significant increase in adrenaline content in the heart. By its nature, sympathetic hyperactivation is accompanied by increased formation of products of enzymatic and nonenzymatic metabolism of adrenaline and its analogs, which can change the use of ATP by cells, change the activity of mitochondrial and cytosolic enzymes, contributing to disruption of bioenergetic adaptation, antioxidant defense system and levels of intercellular modulators such as AMP and adenosine.

AIM: The study objective was to explore the features of adrenaline and its analogs in the regulation of the activity of mitochondrial and cytoplasmic enzymes of cardiomyocytes.

METHODS: The experiment was carried out on 65 3-month-old male Wistar rats weighing 60–190 g. To study the effects of catecholamines and their metabolites in the regulation of mitochondrial and cytoplasmic enzymes activity of cardiomyocytes, experimental rats were put to death by intraperitoneal injection of 10% ketamine in an amount of 0.25 mg/100 g. Activity of mitochondrial succinate dehydrogenase, cytochrome c oxidase, mitochondrial DNP-activated ATPase, adenosine deaminase (AD), AMP deaminase (AMPD), glutathione reductase, and glutathione peroxidase were determined.

RESULTS: Dopamine has the greatest activating effect on cardiac mitochondrial ADH, adrenaline on CHO, and adrenochrome and adrenoxyl on ATPase. Isadrine and dopamine reduce cardiac AMPase activity. An activating effect on cardiac mitochondrial AMPD was found only in norepinephrine.

CONCLUSION: In cardiomyocytes, adrenaline, activates cytosolic enzymes of purine nucleotide metabolism AD and AMPD, as well as increases the level of lipid peroxidation (MDA and DC). This proves that adrenaline acting on adrenoreceptor mechanisms leads the body into a state of oxidative stress. Hormone-mediators of the sympathetic-adrenal system adrenaline, dopamine, noradrenaline, isadrine, and catecholamine metabolites (adrenochrome and adrenoxyl), changes the activity of mitochondrial respiratory chain enzymes of cardiomyocytes, also regulate tissue respiration processes, putting mitochondria into the state of "loose" coupling of respiration and phosphorylation.

Introduction

Catecholamines such as dopamine (DA), norepinephrine (NE), and epinephrine (EPI) are important neurotransmitters and hormones with a variety of essential functions in the body. Besides other functions, catecholamines regulate cardiac action by local neuroendocrine secretion [1].

Already in the 1930's it has been hypothesized that catecholamines might be important regulators of the heart rate even before the inception of neural control [2]. In embryonic chick hearts, catecholamines (NE and EPI) were detected as early as day 3, and L-DOPA and DA were already present from day 1 on [3]. Intrinsic cardiac adrenergic cells were later identified in rat [4], mouse [5], and human [6] heart tissue and primary cardiomyocyte isolates.

Currently, in cardiology, to develop adequate methods for the treatment of cardiovascular diseases, it is highly relevant to establish the mechanisms of disturbances in adaptation processes observed in case

of sympathetic hyperactivation. As many studies show, myocardial ischemia is accompanied by a significant increase in adrenaline content in the heart. By its nature, sympathetic hyperactivation is accompanied by increased formation of products of enzymatic and nonenzymatic metabolism of adrenaline and its analogs, which can change the use of ATP by cells, change the activity of mitochondrial and cytosolic enzymes, contributing to disruption of bioenergetic adaptation, antioxidant defense system and levels of intercellular modulators such as AMP and adenosine.

The control of metabolism and physiological activity of all body cells is carried out by means of a complexly organized specific multifunctional hormonal ensemble [7], [8]. In this regard, for a more meaningful understanding and use of catecholamines in clinical practice, the work set a goal: to study the features of adrenaline and its analogs in the regulation of the activity of mitochondrial and cytoplasmic enzymes of cardiomyocytes. A significant part of the data in this direction has been published by us earlier [9].

Single Nucleotide Polymorphism of Dectin-1 Gene Associates with Atopic Dermatitis in Children

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Abstract

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Keywords: SNP; Dectin-1; Malassezia; Atopic dermatitis; Children

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BACKGROUND: Atopic dermatitis (AD) is a chronic inflammatory skin disease with complex and multifactorial pathophysiology, involving elements of barrier dysfunction, alterations in cell-mediated immune responses, IgE sensitization, and environmental factors. This encourages the search for predictors of disease development among both genetic markers and environment.

AIM: The aim of the study was to examine if genetic factors of Malassezia recognition, or Malassezia colonization may be related to IgE sensitization or to severity of AD.

METHODS: The study included 106 patients with eczema and 103 healthy children. Specific IgE against *Malassezia* mix (m227) was analyzed in 51 patients using immunochemiluminescent method on the ImmunoCAP 100 (Thermo Fisher Scientific Inc., Phadia, Sweden). Genotyping for rs7309123 in Dectin-1 was performed using Real-time PCR. The level of colonization by *Malassezia* in the scale samples was determined by a real-time PCR assay.

RESULTS: Increased IgE to *Malassezia* spp. was observed in 29.4% of children with eczema. Higher *Malassezia* spp. – specific IgE titer positively correlated with severity of AD, age of onset, head-neck type of AD, and a higher total IgE. GG genotype rs7309123 Dectin-1 is significantly more often found in the patients than in the control group, but no correlation with IgE sensitization to *Malassezia* was found. *Malassezia restricta* and *M. globosa* were predominant in patients and controls, with some predominance of *M. globosa* over *M. restricta* among patients.

CONCLUSION: Sensitization to *Malassezia*, genetic markers in Dectin-1, and *Malassezia* colonization of the skin can be tools for studying the gene-environment interactions in the pathogenesis of AD.

Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin disease with a typical characteristic of eczematous lesions. Fungi usually colonize on the skin of AD patients, but the role of these fungi in the pathogenesis of AD remains unclear. The opportunistic yeast *Malassezia* belongs to the normal cutaneous flora. *Malassezia* can also cause IgE-mediated sensitization in patients experiencing AD [1]. IgE, specific for *Malassezia* spp., was found in 5–27% of children [2], [3], [4] and 29–65% of adults with AD [5], [6], [7], [8].

C-type lectin receptor family members are specialized in sensing fungal microbes and linking fungal recognition to the initiation of T-cell responses, in particular those of the Th17 type. Several human studies support the idea that the interaction of Dectin-1 with its ligand promotes the Th2 environment either through instructing naive T-cells, followed by the release of Th2-type cytokines [9], or the release of chemokines (CCL20) associated with a set of Th2 cells [10]. SNP rs7309123 in Dectin-1 showed the strongest association with risk of invasive pulmonary aspergillosis infection [11].

The aim of this study was to identify novel clinical and genetic risk factors for severe AD, accompanied by sensitization to *Malassezia* yeasts. We hypothesized that polymorphism rs7309123 in intron region of Dectin-1 could be associated with childhood eczema and sensitization to *Malassezia* in children with AD. To test this hypothesis, we examined differences in the frequency of this SNP between healthy controls and children with eczema, and the association of polymorphism rs7309123 with IgE to *Malassezia* yeasts.

Materials and Methods

The study included patients with AD ($n = 106$), aged 6 month–18 years (6 [3;10]) from the Department of Allergy at Kyiv City Children Clinical Hospital №2 and 103 children aged 12 month–18 years (6 [5;9]) without the allergic diseases. This study was approved by the Ethical Committee of the O. Bogomolets National Medical University, all patients/parents of the children gave an informed consent to participate.



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Genetic Study of Chemokine Ligand 1 in Colorectal Carcinoma using Quantitative Real-Time PCR

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Abstract

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Introduction

Carcinoma of the colon is one of the most common malignancies and constitutes the third major reason for death due to cancer worldwide [1]. In addition, early diagnosis and molecular characterization are considered essential to decrease colonic carcinoma-related deaths [2]. The 5-year survival rate after curative surgery ranges between 40% and 60% [3]. Nowadays, there are determinate criteria both clinically and pathologically that are usually utilized in choosing the person who is suitable for adjuvant systemic therapy after surgery [4]. Therefore, the definition of prognostic markers in colonic carcinoma is very important in enhancing its prognosis [5]. Several factors either genetically (mutation of P53, KRAS, BRAF, and others genes) or environmentally are involved in the pathogenesis of colorectal carcinoma. The latter is largely dietary, particularly in consumption of a diet rich in fats and animal protein; because they influenced the microflora of the intestine and eventually on the chemical composition of the intraluminal content [3]. Among different factors, chemokines have a prevalent role in the pathogenesis of colonic carcinoma [6]. Chemokine is a small-sized protein manifested in different cells (leukocytes, epithelial

cells, endothelial cells, and fibroblasts), as well as tumor cells [7], [8]. Usually, chemokines are divided into four large categories: C, CC, CXC, and CX3C, depending on the location of their cysteine residues [9]. A previous study revealed that chemokine ligand 1 is overexpressed in some types of human cancer, such as hepatocellular, bladder, prostate, skin cancers, and colorectal carcinoma [10], [11], [12], [13], [14]. CXCL1 plays an axial role in the immune response of the host for bacterial killing by reactivating and recruiting neutrophils at the tissue site [15]. The aim of study is to determine the level of CXCL1 mRNA expression in colonic tumors and to study its correlation with clinic pathological parameters in Iraqi patients.

Materials and Methods

This retrospective study was approved ethically and was carried out in the Department of Pathology, College of Medicine – University of Babylon, Iraq, from January 2017 to August 2019 and the specimens were collected from some general hospitals and some private laboratories in Hilla city.

Role of MicroRNAs in the Development of Chronic Liver Disease in Hepatitis Virus-Infected Egyptian Population

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Abstract

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Keywords: Chronic liver disease; Hepatitis C Virus; Hepatocellular carcinoma; MicroRNAs

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BACKGROUND: The identification of miRNAs that play a role in regulating the viral life cycle and its related liver diseases opens the door for the development of diagnostic biomarkers that can categorize patients at increased risk of developing end-stage liver disease.

AIM: This study investigated the role of miRNAs in the development of viral hepatitis-induced chronic liver disease (CLD) in the Egyptian population, as well as their potential as possible diagnostic biomarkers for chronic hepatitis virus infection.

MATERIALS AND METHODS: The study involved 100 CLD patients; 55 cases of hepatitis C virus (HCV) and 45 cases of non-viral hepatitis, in addition to 40 healthy controls. The expression of five miRNAs (miR-30, miR-122, miR-296, miR-351, and miR-431) was assessed using real-time PCR.

RESULTS: Serum levels of miR-30, miR-122, miR-296, miR-351, and miR-431 were significantly higher in all patients than in the control group ($p < 0.01$). Furthermore, they were significantly greater in viral hepatitis cases compared to the non-viral hepatitis group ($p < 0.01$). The sensitivities and specificities of miR-122a, miR-30, miR-296, miR-351, and miR-431 were (85.71% and 83.33%), (82.35% and 83.33%), (85.71% and 69.44%), (88.64% and 75.76%), and (87.80% and 65.79%), respectively.

CONCLUSIONS: miR-30, miR-122, miR-296, miR-351, and miR-431 play key roles in the development of CLD due to viral infection. Thus, they have the potential to be targeted for the early detection of chronic hepatitis virus infection and allow the exploration of a new frontier in the discovery of innovative therapies to combat chronic viral infection and its serious life-threatening complications, including liver cancer.

Introduction

Despite advances in the development of vaccines and antiviral agents, liver disorders have increasingly become one of the leading causes of death and illness worldwide. Almost 2 million people die per year as a result of major liver illnesses, such as hepatitis virus infections, cirrhosis, and liver cancer, accounting for 4% of all deaths worldwide [1].

One of the key reasons for end-stage liver disease is infection with viral hepatitis, including hepatitis C virus (HCV) and hepatitis B virus (HBV). Understanding the molecular pathways that mediate the chronicity of this infection and its sequelae are required for therapeutic intervention against a variety of life-threatening liver illnesses [2].

The replication of hepatitis viruses, inside the liver cells, differentially disturbs the expression of host miRNAs, which sequentially regulate the virus life cycle by directly targeting its genome and/or cellular signaling pathways, promoting the adaptation, and persistence

of virus infection [3]. Therefore, accumulating evidence reveals that miRNAs could be predictive and prognostic biomarkers, as well as therapeutic targets [4]. More in-depth research on miRNAs associated with and modulating viral infection is indispensable, and their functional role has yet to be clarified [5]. The identification of miRNAs with a prominent role in the viral life cycle and the resulting hepatic disease creates a potential for the development of diagnostic biomarkers that can classify and predict early patients who are at increased risk of developing the end-stage liver disease as a result of viral hepatitis infection [6]. This will also open up a new avenue for the development of novel medications to combat chronic hepatitis virus infection and its devastating repercussions, such as liver cancer.

In the present study, the expression of five miRNAs (miR-30, miR-122, miR-296, miR-351, and miR-431) was analyzed in cases of viral and non-viral induced chronic liver diseases (CLDs) in the Egyptian population to investigate the role of miRNAs and their potential as therapeutic targets against chronic hepatitis virus infection.